

Molecular mechanisms governing hESC and iPS cell self-renewal and pluripotency

Grant Award Details

Molecular mechanisms governing hESC and iPS cell self-renewal and pluripotency

Grant Type: New Faculty II

Grant Number: RN2-00922

Project Objective: The goal of this grant is to gain understanding of the molecular mechanisms governing hESC and iPS cell self-renewal and pluripotency. Additional pursuits, using mESC to inform the hESC studies have been approved through prior approval requests.

Investigator:

Name: Paul Knoepfler

Institution: University of California, Davis

Type: PI

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Cell Line Generation: iPS Cell

Award Value: \$2,157,255

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 5

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Reporting Period: NCE

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Grant Application Details

Application Title: Molecular mechanisms governing hESC and iPS cell self-renewal and pluripotency

Public Abstract: A major problem in regenerative medicine today is that stem cells have the ability to cause tumors and in most cases we currently lack methods to make them safe. For example, two of the most promising stem cells for regenerative medicine, human embryonic stem cells (hESC) and induced pluripotent stem cells (iPS), both readily cause tumors in mice and there is every reason to believe they will do so in humans. The reality is that if we cannot prove that stem cells are safe and do not cause tumors, they will never be used in patients. However surprisingly there is inadequate research into this fundamental problem and it is not funded to a significant degree by the NIH presenting a major gap in the field. In the proposed research we will address this problem by studying why hESC and iPS cells cause tumors and searching for new stem regulators that are safer. Our overall goal is produce safe hESC and iPS cell regenerative medicine therapies. One likely key culprit in the tumor forming capacity of these stem cells is a gene called Myc. Myc is a unique factor in the universe of stem cell regulators because it not only has key roles in the normal, positive functions of many stem cells, but also when found in excess it is one of the most potent cancer-causing genes in humans. Myc has also recently been found to be a critical factor driving iPS cells to form tumors. However, we cannot simply eliminate Myc since it is important for efficient generation of iPS cells and likely for the maintenance of the positive properties of stem cells, including hESC, needed for regenerative medicine. In order to achieve our goal to enhance the safety of stem cells without sacrificing our ability to efficiently generate them or their key functions, we will take two main approaches in the proposed research. The first is to study how Myc works in iPS cells and hESC in order to find methods to enlist the positive effects while eliminating the negative properties. Remarkably, there is currently no information on how Myc functions in iPS cells and hESC. The second is to screen in a global, unbiased manner for new stem cell factors that can substitute for Myc or enhance iPS function independent of Myc. When these studies are successfully completed we will for the first time know the factors responsible for inducing stem cells to cause cancer, paving the way for eliminating that function, and we will have discovered new stem cell regulators that have better profiles of safety and efficacy than existing factors such as Myc. Together these achievements will bring us much closer to using the vast potential of iPS and hESC for new therapies that are both safe and effective. Longer term our goal is to work with our neural (Alzheimer's disease, Parkinson's disease, and spinal cord injury), cardiac, and liver disease teams here to generate safe and effective stem cell based therapies tailored for each patient.

Statement of Benefit to California: Enhancing the safety of regenerative medicine therapies will be of great benefit to the State of California both in terms of improving the lives of patients, by removing arguably the most serious roadblock to regenerative medicine, as well as enhancing the knowledge of the stem cell field. It will also further the development and clinical use of regenerative medicine leading to a new, valuable biotechnology. California should be a leader in developing safe, effective regenerative medicine.

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